

inhibiting TNF-alpha and IL-1beta associated inflammatory pathways and activating TNFR2 and Integrin associated chondro-protective pathways (Fig 3).

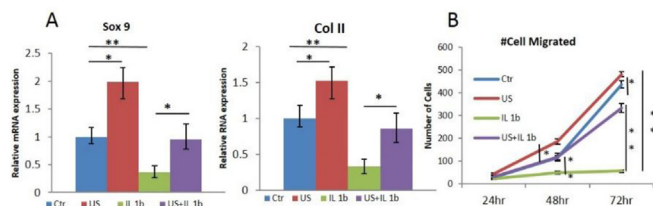


Fig 1A. LIPUS enhances chondrogenesis and neutralizes IL-1beta B) LIPUS restores IL-1beta induced chondrocytes migration inhibition.

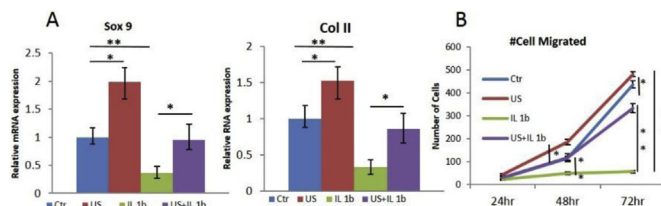
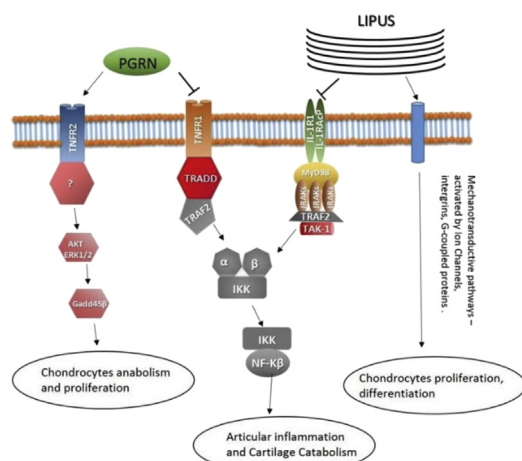


Figure 2. A) combine treatment of PGRN and LIPUS show synergistic effects in chondrocytes anabolism. B) LIPUS +PGRN treatment enhances saffron O staining and protect against cytokines induce cartilage degradation.



subcutaneous adipose tissue (SAT; 9 donors) were used to make conditioned medium (CM). Additionally, CM was made of macrophages derived from peripheral blood monocytes of 3 donors. The effect of different types of CM on chondrogenesis of 3 human bone marrow-derived MSC donors was evaluated by gene expression, biochemistry and immunohistochemistry.

Results: CM from both IPFP sources and pro-inflammatory macrophages significantly decreased gene expression of collagen type 2 (COL2A1; $p<0.01$) and aggrecan (ACAN; $p<0.05$), the COL2/collagen type 1 (COL1A1; $p<0.01$) and ACAN/versican ratio ($p<0.05$). CM from SAT only significantly decreased COL2A1 ($p=0.01$) and not ACAN. There was no significant difference between CM from TKR and ACL IPFP donors and there was no difference between CM from lean (BMI<25) or obese (BMI>30) IPFP donors. GAG deposition, evaluated by DMMB assay, was not influenced by IPFP CM. Immunohistochemistry showed a decrease in collagen type 2 staining by IPFP CM, whereas collagen type 1 staining was not influenced.

Conclusions: Factors secreted by the IPFP from diseased joints inhibit chondrogenesis of MSCs and shift production of hyaline cartilage matrix to a fibrocartilage matrix. Type of joint pathology and obesity do not influence this effect. The IPFP and its macrophages could be a target for future therapies to improve the results of the microfracture procedure in the knee.

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MIR-455 INDUCES CHONDROGENESIS BY INHIBITING RUNX2

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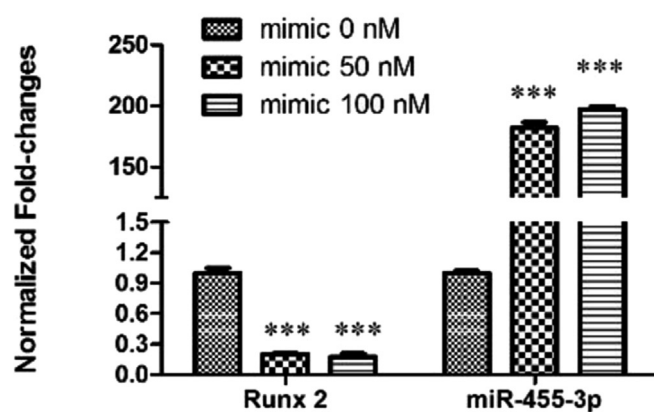
Purpose: The expression of miR-455-3p was significantly up-regulated in the chondrogenesis of mesenchymal stem cells, but its role still remains unknown in different stage during chondrogenesis. Here, we have investigated the function of miR-455-3p in chondrogenesis, and generated a picture of the relationship with Runx2.

Methods: Chondrogenic ATDC5 cells were used. The expression of miR-455-3p, Runx2 and related genes were tested by quantitative real-time polymerase chain reaction (qPCR), and in situ hybridization. The function of miR-455-3p in chondrogenesis and its regulation on Runx2 were examined by over-expressed and knocked down miR-455-3p by miR-455-3p mimic and inhibitor treatments and luciferase assay. The expression of miR-455-3p and related genes in ATDC5 after 14 d chondrogenic induction was investigated with or without IL-1 β stimulation.

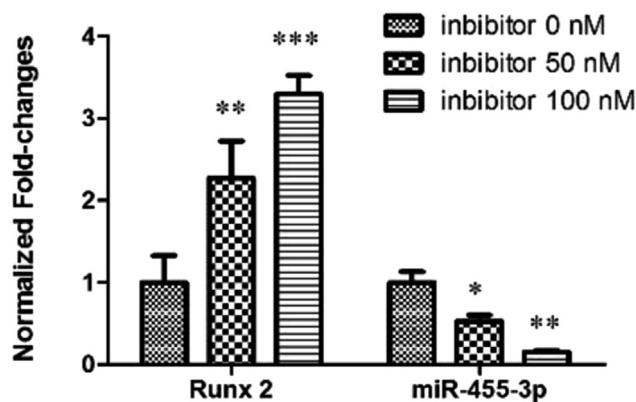
Results: MiR-455-3p was increased in ATDC5 from 0 d to 21d, but then rapidly decreased, and the same expression kinetics was detected in the development of mouse embryos. The expression level of Runx2 was steadily increased before 21 d, then significantly increased in 28 d which miR-455-3p was rapidly decreased. Furthermore, miR-455-3p functions as an activator for the early chondrogenic differentiation from the results of Col2a1, COMP and Adamts-5 expression after over-expressed and knocked down miR-455-3p, and this activation of miR-455-3p was potentially through inhibited the function of Runx2. On the other hand, IL-1 β could stimulate the expression of miR-455-3p and C/EBP β in ATDC5 after 14 d chondrogenic induction.

Conclusions: MiR-455-3p has a critical role in the early chondrogenesis as an activator by the regulating Runx2. MiR-455-3p has a potential function in cartilage degeneration during hypertrophic differentiation. Our results indicates that miR-455-3p potentially alter the chondrogenic differentiation.

A



B



C

